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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,980	07/17/2000	RICHARD KOLESNICK	D6049	6671

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EXAMINER
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ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No. 09/554,980	Applicant(s) FUKS et al.
	Examiner Fozia Hamud	Art Unit 1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 15, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6, 7, and 10* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6, 7, and 10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

1. Receipt of Applicant's arguments and amendments filed in Paper No.10 filed on 15 April 2002 is acknowledged. Claims 1, 4 and 10 are amended and claim 5 is canceled.

Thus claims 1-4, 6-7 and 10 are pending and under consideration by the Examiner.

2. The following previous rejections and objections are withdrawn in light of Applicants amendments filed in Paper No.10, 4/15/02:

(I) All of the rejections against claim 5 are moot, since this claim has been canceled.

(ii) The rejection of claims 1, 4 and 10 under 35 U.S.C §112, second paragraph for reciting "pharmacologically effective dose".

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 1 is vague and indefinite for reciting ".....an animal in need of such treatment....", however, it is not clear which animal is in need of such treatment. Appropriate correction is required.

Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being vague and indefinite insofar as they depend on claim 1 for the "..an animal in need of such treatment" limitation discussed above.

Claim Rejections - 35 U.S.C. § 102

5. The rejection of claims 1, 4, made under 35 U.S.C. 102(b) as being anticipated by Fuks et al (1994), is maintained for reasons set forth n the office action mailed on 27 February 2002, in paper No:9, pages 4-5.

Applicants argue that Fuks et al did not teach or suggest using b-FGF to inhibit the generation of ceramide from sphingomyelin, nor using b-FGF to treat endotoxic shock as claimed in the instant application. Applicants further argue that Fuks et la did not teach or suggest that the administration of b-FGF would inherently lead to inhibition of ceramide generation from sphingomyelin, in contrast, Fuks et al teach and suggest that b-FGF activates membrane protein kinase C, as a mechanism for resistance to radiation damage and apoptosis. Thus, Applicants conclude that since Fuks et al does not teach or suggest each and every aspect of the instant invention, this reference does not anticipate instant claims 1 and 4.

These arguments have been fully considered but are not deemed persuasive.

Firstly, Fuks et al reference does teach that the administration of basic fibroblast growth factor (b-FGF) to an animal leads to the inhibition of radiation-induced endothelial cell death (endothelial apoptosis), (see abstract, pages 2585-2586, column 2 and figure 7). Thus, although, Fuks et al reference does not expressly teach that the administration of b-FGF leads to the inhibition of the generation of ceramide from sphingomyelin, this is an inherent property of the administration of b-FGF. The discovery of an inherent property of a prior art process can not serve as a basis of patenting that process, see Ex parte Novitski, 26 USPQ2d (Bd. Pat. App. & Inter. 1993). In the instant case, the administration of b-FGF into a mammal to protect said animalfrom apoptosis is in the prior art of record. Applicants have delineated the mechanism of action of said process by

showing that b-FGF inhibits the generation of ceramide from sphingomyelin. However, this is not a patentable contribution over the prior art process. With respect to Applicants' argument that Fuks et al teach and suggest that b-FGF activates membrane protein kinase C, as a mechanism for resistance to radiation damage and apoptosis, rather than inhibiting ceramide from sphingomyelin as claimed in the instant case, the administration of b-FGF for what ever reason, would inherently, by its properties inhibit the generation of ceramide. Therefore, it does not matter whether Fuks et al teach or suggest a different mechanism of action.

Instant claim 1 is drawn to a method of administering b-FGF to an animal to inhibit ceramide generation form sphingomyelin, and claim 4 adds the limitation that said administration of b-FGF prevents endothelial apoptosis resulting from endotoxic shock by inhibiting ceramide generation from sphingomyelin. Fuks et al reference expressly teaches the administration of b-FGF into an animal, it also teaches that said administration inhibits endothelial apoptosis. Therefore, Fuks et al reference does teach all the limitations in instant claims 1 and 4, either expressly or inherently, thus, anticipating instant claims 1 and 4. Whether the reference teaches the mechanism of action claimed by Applicants or a different mechanism of action for b-FGF is irrelevant, as long as the reference teaches the claimed method, which it does, thus anticipating instant claims 1 and 4.

New Rejections:

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al (1994).

Fuks et al teach a method of administering basic fibroblast growth factor (b-FGF) into an animal to inhibit radiation-induced programmed cell death *(endothelial apoptosis) in-vitro* and *in-vivo*. The researchers using C3H/HeJ mice exposed to lethal dose of whole lung irradiation which exhibited similar apoptotic changes in the endothelial cell lining of the pulmonary microvasculature within 6-8 hours of radiation exposure, showed that b-FGF given intravenously immediately before and after irradiation inhibited the development of apoptosis in these cells and protected mice against development of lethal radiation pneumonitis, (see abstract, pages 2585-2586, column 2 and figure 7).

Instant claim 10 is drawn to a method of treating sepsis by administering b-FGF. Therefore, the Fuks et al reference anticipates instant claim 10, because it teaches the administration of b-FGF into an animal. The administration of b-FGF would inherently lead to the inhibition of ceramide generation from sphingomyelin, and would lead to the treatment of sepsis, because a product's function is an inherent property of its structure.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1, 4 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Hamivotiz-Friedman et al (1 December 1997).

Haimovitz-Friedman et al teach a method of inhibiting LPS-induced ceramide elevation, endothelial apoptosis and animal death by administering b-FGF to an animal, (see abstract and page 1836, column 1, second paragraph). Haimovitz-Friedman et al disclose that LPS leads to endothelial apoptosis, mediated sequentially by TNF-α and ceramide generation and that b-FGF abrogated this LPS induced apoptosis, (see page 1836). The researchers propose that the inhibition of ceramide generation by b-FGF may affect the progression of the LPS syndrome in patients already manifesting symptoms of septic shock, (see page 1839, last paragraph).

Instant claim 1 is drawn to a method of administering b-FGF to an animal to inhibit ceramide generation from sphingomyelin and claim 4 adds the limitation that said administration of b-FGF prevents endothelial apoptosis resulting from endotoxic shock by inhibiting ceramide generation from sphingomyelin. Claim 10 is drawn to a method of treating sepsis by administering b-FGF.

Therefore, since Haimovitz-Friedman reference teaches the administration of b-FGF into an animal, and that said administration leads to the inhibition of LPS- induced ceramide generation which affects the progression of the LPS syndrome in patients already manifesting symptoms of septic shock, the Haimovitz-Friedman reference anticipates instant claims 1, 4 and 10.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

8. Claims 1, 2, 3, 4, 6 and 7 are rejected under U.S.C. § 103 as being unpatentable over Fuks et al (1994).

The teachings of Fuks et al have been set forth above, as applied to claims 1, 4 and 10. However, Fuks et al do not disclose a method of administering b-FGF to a human or a method of administering b-FGF into an animal using the doses and times recited in claims 3 and 7.

Fuks et al teach a method of administering b-FGF into an animal to inhibit endothelial apoptosis. The researchers showed that administration basic fibroblast growth factor (b-FGF) into an animal leads to the inhibition of radiation-induced programmed cell death *(endothelial apoptosis) in-vitro* and *in-vivo*.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention, to design a method of administering b-FGF into a human and to optimize both the dosage and duration of said administration to get the benefits of this protein, because Fuks et al taught that b-FGF inhibits endothelial apoptosis. One of ordinary skill in the art would have been motivated to administer b-FGF to a human and to optimize the duration and the dosage, because, many pathological conditions, including endotoxic shock lead to endothelial apoptosis which leads to the death of the patient, and saving patients is always the ultimate goal of the medical field.

Conclusion

9. No claim is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Mondays and Thursdays and every other Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary kunz can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Art Unit: 1647

Fozia Hamud
Patent Examiner
Art Unit 1647
12 June 2002

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